68. The method according to claim 66 wherein said anti-fibrotic agent is said molecule and said molecule is an antibody or a soluble form of said receptor.

69. The method according to claim 68 wherein said antibody is an anti-TGF-β_1, anti-TGF-β_2 or anti-PDGF antibody.

70. The method according to claim 64 wherein said TGF-β_3 is provided at said site in an inactive form that is converted to an active form at said site.

Claim added

71. The method according to claim 64 wherein said TGF-β_3 is provided at said site in a pharmaceutical composition comprising a pharmaceutically acceptable carrier.--

REMARKS

Reconsideration of the above-identified application and entry of the foregoing amendments are respectfully requested.

The undersigned wishes to express appreciation to the Examiner for the very constructive interview of October 27, 1998. The Examiner's remarks on the PTO-413 Form adequately summarize the interview and thus no further comment is believed necessary.

All of the previously presented claims have been cancelled and new claims 56-71 have been added in lieu thereof. As

indicated on the Examiner's Interview Summary, draft claim language was shown at the time of the interview. New claims 56 and 64 correspond to claims 56 and 57, respectively, shown at the interview. The new claims, which are fully and clearly supported by an enabling disclosure (including the claims as originally filed), are believed to define the invention with additional clarity. That the claims have been revised should not be taken as an indication that Applicants agree with any view expressed by the Examiner. Rather, the revisions are made in order to advance prosecution and Applicants reserve the right to pursue any deleted subject matter in a continuation application.

The invention as now claimed relates to a method of inhibiting fibrosis and to a method of reducing scarring during wound healing. The methods comprise providing TGF-β_3 in an amount sufficient to effect the inhibition and reduction in scarring, respectfully. The invention is based on Applicants' wholly unexpected discovery that TGF-β_3 is distinct from TGF-β_1 and TGF-β_2 in that TGF-β_3 is an anti-fibrotic growth factor while TGF-β_1 and TGF-β_2 are fibrotic growth factors (see the Experiments beginning at page 8 of the application and the summary thereof provided in the paragraph bridging pages 14 and 15). Prior to the present invention, it was believed that the three forms of TGF-β, which are structurally homologous, were

functionally equivalent. The primary references upon which the Examiner relies fully support this assertion.

Applicants turn now to the specific points raised by the Examiner in the Office Action dated December 9, 1997, and offer the following further comments, bearing in mind the nature of the claims as now presented.

On page 2 of the Action, the Examiner rejects claims 1, 4 and 5 under 35 USC 112, first paragraph. The rejected claims are drawn to a composition. Those claims have now been cancelled and no further composition claims have been presented. Accordingly, the rejection is rendered moot.

Also on page 2 of the Action, the Examiner rejects claims 1 and 4-22 under 35 USC 102(b) as allegedly being anticipated by Ammann et al. Withdrawal of the rejection is submitted to be in order in view of the cancellation of the rejected claims. The newly presented claims are not anticipated by the reference for the reasons that follow.

Ammann et al relates to a TGF-β-containing composition suitable for use in

> the treatment periodontitis which is effective in both supragingival and subgingival treatment. The composition is also capable of restoring the regrowth of the periodontium, including alveolar bone and of the periodonal connective tissue, and reducing the release of additional collagenase.

(see column 14, lines 7-14).

The term "TGF-β" is defined in the Ammann et al specification as referring to any of TGF-β_1, TGF-β_2 and TGF-β_3. No distinction between the 3 forms, in terms of function for the recited purpose, is seen in the citation - Examples 2 and 3 refer only to TGF-β_1.

As pointed out above, the present invention results from Applicants' realization that TGF-β_3, unlike TGF-β_1 and TGF-β_2, is an anti-fibrotic growth factor. Ammann et al is clearly devoid of any suggestion of such a distinction. Indeed, Ammann et al equates the 3 forms in terms of their effectiveness for the treatment taught. Accordingly, nothing in Ammann et al can be said to have suggested the present invention. Reconsideration is thus requested.

Claims 1, 2, 6, 12 and 14-22 stand rejected under 35 USC 102(b) as allegedly being anticipated by Cerletti et al. Withdrawal of the rejection is submitted to be in order in view of the cancellation of the rejected claims. The new claims are not anticipated by the reference for the reasons that follow.

Cerletti et al relates to TGF-β-containing compositions and to the use thereof in the promotion and acceleration of wound healing and bone and tissue repair, etc (see page 2, lines 2-6). The term "TGF-β-like protein" is indicated as including TGF-β_1, TGF-β_2 and TGF-β_3. As in the case of Ammann et al, no

distinction between the three forms, in terms of function for the recited purpose, is found in Cerletti et al - the wound healing example, in fact, utilizes TGF-β_2.

Again, the present invention is based on Applicants' realization that TGF-β_3, in contrast to TGF-β_1 and TGF-β_2, is an anti-fibrotic growth factor. Cerletti et al says nothing of any such distinction. On the contrary, Cerletti et al, like Ammann et al, equates the 3 forms in terms of their appropriateness for the treatment taught. Accordingly, nothing in Cerletti et al would have suggested the presently claimed methods and reconsideration is thus requested.

Claims 1 and 3 stand rejected under 35 USC 103 as allegedly being obvious over Cerletti et al or Ammann et al in view of Baird et al. Withdrawal of the rejection is submitted to be in order in view of the cancellation of the rejected claims. The new claims would not have been obvious of the combination for the reasons that follow.

The failings of the primary references are discussed in detail above. Nothing in the Baird et al teaching of FGF would have cured that deficiency. Accordingly, reconsideration is requested.

This application is submitted to be in condition for allowance and a Notice to that effect is requested.

FERGUSON et al -- Serial No. 08/307,640

Respectfully submitted,

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